REMARKS

Claims 1-58 are pending in this application. Claims 1-11, 15-27 and 38-58 were withdrawn from consideration in response to a restriction requirement. Accordingly, claims 12-14 and 28-37 are currently subject to examination.

Claims 12-14 and 28-37 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to practice the full scope of the invention. Claims 12-14 and 28-37 also stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Claims 12-13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Liversidge et al., U.S. Patent No. 6,221,400 ("Liversidge"). Claims 12-14 and 28-37 also stand rejected under 35 U.S.C. § 103 as being unpatentable over Semenov (Antimicrobial Agents and Chemotherapy 42, 2254-2258, 1998) or Davis, U.S. Patent No. 5,278,173 ("Davis"), in view of Patel, U.S. Patent No. 6,265,406 ("Patel") or Johnson, U.S. Publication No. 2002/0177603 ("Johnson").

Claims 12, 14 and 28 are amended and claims 13, 29 and 30 are cancelled.

Claim 12 has been amended by clarifying that the method of the present invention is used to treat malaria in humans and by adding the limitations of claim 13 regarding the protease inhibitors that may be administered in the method. Claim 14 has been amended to correct a grammatical error. Claim 28 has been amended by clarifying that the method of the present invention is used to treat HIV infection, malaria or both in humans and by adding the limitations of claims 29 and 30 regarding the quinolic compounds and protease inhibitors that may be administered in the method. No new matter has been added.

Claims 12 and 14 recite one embodiment of the present invention in which a therapeutically effective amount of an HIV protease inhibitor is administered to a person in need of treatment for malaria. As recited in claim 12, the HIV protease inhibitor is selected from the group consisting of indinavir (IDV), ritonavir (RTV), saquinavir (SQV), nelfinavir (NFV), lopinavir (LPV), amprenavir (APV), fosamprenavir, tipranavir, atazanavir, TMC-114, and combinations thereof. Pharmaceutically acceptable salts of these protease inhibitors may also be used in the method of amended claim 12. Claim 14 recites a specific embodiment of the invention in which ritonavir is administered at a dose of between about 1 mg per kg of body weight to about 150 mg per kg of body weight. As described in the specification at, for example, paragraphs 0063 and 0064, the HIV protease inhibitors exhibit antimalarial effects. As demonstrated in Examples II and III of the specification, these antimalarial effects are observable in vitro and in vivo.

Claims 28 and 31-37 as amended recite an embodiment of the invention in which a combination of a quinolic compound and an HIV protease inhibitor are administered to a patient in need of treatment for HIV infection, malaria, or both. As recited in amended claim 28, the quinolic compound is selected from the group consisting of chloroquine, hydroxychloroquine, mefloquine, quinine and combinations thereof. The HIV protease inhibitor is selected from the group consisting of indinavir, ritonavir, saquinavir, nelfinavir, lopinavir, amprenavir, fosamprenavir, tipranavir, atazanavir, TMC-114 and combinations thereof. Claims 31-32 recite embodiments of the invention in which a nucleosidic inhibitor of the HIV Reverse Transcriptase (NRTI) compound is also administered. Claims 33-37 recite specific amounts of the quinolic compounds or HIV protease inhibitor in the combinations used in the methods.

As described in the specification at, for example, paragraphs 0047-0050, administration of the combination of an HIV protease inhibitor with an anti-malarial compound such as chloroquine can restore sensitivity to HIV protease inhibitors (PIs) in strains of HIV virus that are resistant to PIs. In addition, use of a quinolic compound in combination with a PI can reduce the effective dose of the PI required to treat the HIV infection. This can decrease the cost of the treatment and reduce possible toxicity associate with administration of PIs.

As further described in the specification at, for example, paragraphs 0051 and 0090-0091, administration of a combination of a quinolic compound, such as chloroquine, with a PI exhibits a synergistic effect in the treatment of *P. falciparum* strains of malaria.

Rejection Under 35 U.S.C. §112, first paragraph (Enablement)

Claims 12, 14, 28 and 31-37 stand rejected under 35 U.S.C. §112, first paragraph as containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to use the full scope of the claimed invention. At pages 2-3 of the office action, the examiner states that "the specification, while being enabling for treating malaria using the compounds as claimed, does not reasonably provide enablement for preventing malaria using combinations of HIV protease inhibitors as claimed." Independent claims 12 and 28 have been amended to delete "preventing". Accordingly, the claims now recite a method for treating malaria, which as the examiner has pointed out, is enabled by the specification. Applicant respectfully asserts that the description in the specification and examples provided enable the full scope of the invention as recited in the amended claims.

Rejection Under 35 U.S.C. §112, first paragraph (Written Description)

Claims 12, 14, 28 and 31-37 stand rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. The examiner states at page 7 that the term "inhibitor of the HIV protease" is not sufficiently described in the specification to cover the entire claimed genus.

Independent claims 12 and 28 have been amended to recite the specific PIs described in the application as filed. The recitation in the amended claims is fully supported by the description in the specification. Accordingly, the rejection for failure to meet the written description requirement should be withdrawn.

Rejection of Claim 12 Under 35 U.S.C. §102(b) Based Upon Liversidge

Claim 12 stands rejected under 35 U.S.C. §102(b) based upon Liversidge, U.S. Patent No. 6,221,400. Liversidge is directed to compositions comprising nanoparticulate HIV protease inhibitor drug substances having a cellulosic surface stabilizer. According to Liversidge, the nanoparticulate formulations have an increased rate of dissolution in vitro and an increased rate of absorption in vivo. Liversidge describes the use of the nanoparticulate HIV protease inhibitors for treatment of HIV infections.

The Examiner has rejected the claims as "illustrating anticipation resulting from inherent use", citing Ex Parte Novitski, 26 U.S.P.Q. 2d 1389 (Bd. Pat. Appeals & Int. 1992). The Novitski decision, which the Board explicitly limited to the particular facts of that case, held that a prior art reference which described inoculating a plant with a bacteria described in the reference as having "broad spectrum anti-fungal activity" anticipated claims to a method of using the bacteria to inoculate plants against nematodes, a particular type of fungus. Liversidge does not describe or suggest the use of PIs for treatment of malaria. Liversidge only describes and

claims the use of nanoparticulate protease inhibitors for treatment of HIV infections. Because Liversidge does not even hint at the use of the protease inhibitors for treatment of malaria, the present case is very different from the Novitski case, where the prior art reference broadly described the use of the bacteria for inoculation against fungus and the claimed invention was for inoculation against a specific type of fungus.

The claims as amended recite methods for treating malaria by administering PIs to a person in need thereof, i.e. a person in need of treatment for malaria. The Examiner has incorrectly stated that the recitation in the preamble is a statement of intended use. The claims as amended recite, after the transition phrase "comprising", a method of treating a person *in need thereof* with the protease inhibitors recited in the amended claim. The recitation "in need thereof" in the body of the claim refers back to the preamble, which recites that the method is for treating a person for malaria. In Jansen v. Rexall Sundown, 342 F.3d 1329, 1333 (Fed. Cir. 2003), the Federal Circuit made clear that claims in this format are not merely statements of intended use:

> In both Rapoport [v. Dement, 254 F.3d 1053 (Fed. Cir. 2001)] and this case, the claim preamble sets forth the objective of the method, and the body of the claim directs that the method be performed on someone "in need". In both cases, the claims' recitation of a patient or a human "in need" gives life and meaning to the preambles' statement of purpose. . . .The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed.

In order to anticipate a claim under 35 U.S.C. § 102, all of the limitations of the claim must be disclosed in a single prior art reference. MPEP § 2131; Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987); Lewmar Marine Inc. v. Barient, Inc., 827 F.2d 744, 747 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 1007 (1988). Moreover, the single source

must disclose all of the claimed elements "arranged as in the claim." Structural Rubber Prods. Co. v. Park Rubber Co., 749 F.2d 707, 716 (Fed. Cir. 1984). Liversidge does not disclose the use of protease inhibitors to treat malaria. Accordingly, Liversidge does not anticipate claim 12 as amended under 35 U.S.C. § 102 for at least this reason.

Rejection of Claims 12, 14, 28 and 31-37 Under 35 U.S.C. §103

Claims 12, 14, 28 and 31-37 stand rejected under 35 U.S.C. § 103 as being unpatentable over Semenov (Antimicrobial Agents and Chemotherapy 42, 2254-2258, 1998) or Davis, U.S. Patent No. 5,278,173 ("Davis"), in view of Patel, U.S. Patent No. 6,265,406 ("Patel") or Johnson, U.S. Publication No. 2002/0177603 ("Johnson").

Semenov describes the use of combinations of cysteine protease inhibitors and aspartic protease inhibitors in the treatment of *P. falciparum*, i.e. malaria. The cysteine protease inhibitors E-64 (L-Transepoxy-succinyl-leucylamido-(4-guanidino)-butane) and vinyl sulfone were used in combination with pepstatin, an aspartic protease inhibitor. Semenov does not describe, teach or suggest the use of any of the HIV protease inhibitors recited in claim 12 as amended to treat malaria. As noted by the Examiner, treatment of malaria is unpredictable, and there is nothing in Semenov that suggests the use of HIV protease inhibitors for the treatment of malaria. Moreover, Semenov does not describe the combination of HIV protease inhibitors with the quinolic anti-malarials as recited in claim 28 as amended, and Semenov does not describe or recognize the synergistic effect of the combination in the treatment of malaria or HIV infection.

Davis describes the use of certain anti-malarial compounds, including chloroquine, for treatment of HIV infection. Davis does not describe, teach or suggest the use of HIV protease

inhibitors for treatment of malaria as recited in claim 12 as amended. Moreover, Davis does not teach or suggest administering a combination of a quinolic anti-malarial with a protease inhibitor for treatment of either malaria or HIV infection as recited in claim 28 as amended, and Davis does not describe or recognize the synergistic effect of the combination in the treatment of malaria or HIV infection.

Patel does not address the deficiencies in Semenov or Davis. Patel describes substituted quinolin-2 (1H) -ones for use as inhibitors of HIV reverse transcriptase. The structures of the molecules described in Patel are shown as Formula I (col. 4, line 22 -col. 6, line 8), or Formula II (col. 6, line 11 - col. 10, line 6). None of the molecules described in Patel are chloroquine, hydroxychloroquine, mefloquine or quinine, the anti-malarials recited in claim 28 as amended. Patel does not describe treatment of malaria at all, much less describe the use of HIV protease inhibitors for the treatment of malaria as claimed in claim 12 as amended. Moreover, because Patel does not describe any of the quinolic compounds recited in claim 28, Patel does not teach or suggest the use of those compounds in combination with a protease inhibitor for the treatment of HIV infection, malaria or both, nor does Patel describe or recognize the synergistic effect of the combination in the treatment of malaria or HIV infection. Accordingly, the combination of Patel with either Semenov or Davis does not result in the invention of claims 12, 14, 28 and 31-37 as amended, and the claims are patentable over the combinations for at least this reason.

Johnson describes tricyclic compounds which may be used as inhibitors of HIV reverse transcriptase. Johnson does not describe treatment of malaria at all, much less treatment of malaria using the HIV protease inhibitors recited in claim 12 as amended. Moreover, Johnson does not describe, teach or otherwise suggest the use of the quinolic compounds in combination with the HIV protease inhibitors recited in amended claim 28 for treatment of HIV infection,

malaria or both, nor does Johnson describe or recognize the synergistic effect of the combination in the treatment of malaria or HIV infection. Accordingly, the combination of Johnson with either Semenov or Davis does not result in the invention of claims 12, 14, 28 and 31-37 as amended, and the claims are patentable over the combinations for at least this reason.

As recognized by the Examiner in the Office Action, treatment of malaria and HIV infection is unpredictable. The inventor has discovered that certain HIV protease inhibitors are effective in treating malaria, and has also discovered that the combination of certain quinolic anti-malarials in combination with certain protease inhibitors can provide synergistic effects in the treatment of both malaria and HIV infection. As discussed above, the combination of the references cited by the Examiner does not result in the treatment methods in any of claims 12, 14, 28 or 31-37 as amended, and the claims as amended are patentable over the references cited by the Examiner for at least the reasons given above.

In view of the amendments to the claims and the foregoing remarks, the pending claims are believed to be allowable over the prior art of record. Accordingly, it is respectfully requested that this application be allowed and a Notice of Allowance issued. If the Examiner believes that a telephone conference with Applicants' attorney would be advantageous to the disposition of this case, the Examiner is cordially requested to telephone the undersigned. If the Examiner has any questions in connection with this paper, or otherwise if it would facilitate the examination of this application, please call the undersigned at the telephone number below.

Because the reasons above are sufficient to traverse the rejection, Applicants have not explored, nor do they now present, other possible reasons for traversing such rejections. Nonetheless, Applicants expressly reserve the right to do so, if appropriate, in response to any future Office Action.

Serial No. 10/783,268 Docket No. 97728.00147

A Petition for a Two Month Extension of Time and the associated fee have been field herewith, extending the time to respond until January 21, 2008. Because the office was closed for a holiday on January 21, this paper is timely filed on January 22, 2008. No additional fee is believed to be required. However, if any fee is required, or otherwise if necessary to cover any deficiency in fees already paid, authorization is hereby given to charge our Deposit Account No. 50-3569.

Respectfully submitted,

Date: January 22, 2008

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